

GCCAGGTCTGGCACCATGCACTAGGATACCCAGAACGCTGCAAGGCCACGCC
CTCCTCACTTCAGGGGTCACTCTCCCCATTGCCACCACCCACCATGGCTGGG
GATCGGCTCCCGAGGAAGGTGATGGACGCAAAGAACTGGCCAGCCTGCTGC
GTGGCGGGCCTGGGGGACCCCTTGGTCATCGACAGCCGGTCCTTCGTGGAGTAT
AACAGCTGCCACGTGCTGAGCTCTGTGAATATCTGCTGTTCAAAGCTGGTGAA
GCGGCGCCTTCAGCAGGGGAAAAGTGACAATTGCTGAGCTTATCCAGCCTGCTA
CACGGAGCCAGGTGGATGCCACAGAACACAGGATGTAGTGGTGTATGACCA
GAGCACACGAGATGCCAGCGTGCTGGCAGCAGACAGCTTCCTGTCCATCCTGC
TCAGCAAGCTGGACGGCTGCTTCGACAGTGTGGCCATCCTCACAGGAGGCTTC
GCCACCTTCTCCTCCTGCTTCCCTGGCCTCTGTGAGGGCAAGCCTGCCACTCTA
CCGTCCATGAGCCTCTCTCAGCCCTGCCTGCCTGTGCCCAGTGTGTCCTGACC
CGAATCCTGCCTCACCTCTACCTGGGCTCTCAGAAAGATGTCTTGAACAAGGA
TCTGATGACCCAAAACGGAATAAGCTATGTCCTCAATGCCAGCAACTCCTGCC
CTAAACCGGACTTCATCTGTGAGAGCCGTTTCATGCGTATCCCCATCAATGAC
AACTACTGTGAAAAGCTGCTGCCCTGGCTGGACAAGTCCATCGAGTTTATTGA
TAAAGCCAAGCTGTCCAGCTGCCAAGTCATTGTTCACTGTCTGGCTGGCATCTC
TCGCTCTGCCACCATTGCCATCGCGTACATCATGAAAACCATGGGCATGTCTTC
TGACGACGCATACAGGTTTGTGAAGGATCGGCGCCCCTCCATCTCGCCCAACT
TCAACTTCCTGGGCCAGTTGCTGGAGTATGAGAGGAGTCTGAAGCTGCTGGCT
GCCCTGCAGACTGATGGACCTCACTTGGGGACCCCTGAGCCCCTCATGGGCCC
GGCAGCAGGCATCCCACTGCCCCGGCTGCCACCATCTACCTCAGAGAGCGCTG
CCACTGGGAGCGAGGCAGCCACCGCAGCCAGGGAGGGCAGCCCAAGTGCTGG
AGGGGATGCTCCGATCCCCAGCACAGCTCCAGCCACCAGCGCGCTGCAGCAG
GGCCTGCGTGGCCTGCACCTCTCCTCTGACCGCCTCCAGGACACCAACCGCCT
CAAGCGTTCCTTTTCCCTGGACATCAAGTCGGCCTATGCACCCAGCAGGAGGC
CCGACTTTCCCGGCCACCCGACCCCGGTGAAGCCCCGAAGCTCTGCAAGCTG
GACAGCCCGTCTGGGGGCACACTGGGCCTGCCCTCGCCAGCCCAGACAGCCC
GGACTCCGTTCCAGAGTGCCGCCCACGACCCCGCCGGCGACGCCCCCGGCTA
GTTTCGCTGCCCCGCTCCCCCGCGCATGGTCTGGGCCTGAACTTTGGAGACACG
GCCCCGAGACTCCACGGCACGGCCTCTCGGCCCTGTGCGCGCCCGGGCTGCC
TGGCCCTGGCCAGCCGGCTGGCCCCGGGGGCTGGGTGCCGCCACTGGACTCCC
CAGGCACACCGTCGCCCCGACGGCCCCCTGGTGCTTCAGCCCCGAGGGCGCGCA
GGGTCCAGGCGCTGTGTTCTCCGCCTTTGGCCGGGTAAAGTGCAGGCGCACCTG
GACCCGGTAACAGCAGCAGCAGCGGTGGTGGTGGTGGTGGTGGTGGCGGCGG
CGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGG
CAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAG
CGGAGGCGGGATGTGCGGACCGGCTGGCCCCGAGGAGCCTGCTGCAGATGCAC
AGTTCAAGAGGCGCAGCTGCCAGATGGAGTTCGAAGAGGGCATGGTGGAGGG
GCGGGCACGTGGCGAGGAGCTGGCAGCCCTGGGCAAGCAAACCAGCTTCTCT
GGCAGCGTGAGGTTCATCGAAGTATCGTGACCCTTCAGAAGTCCCTGTGCCCT
TGCTCCAGCCAGGCCAGGTATAAATATATATTATATATAAAACACACAGAAAA
GGTAAATGGTTTTACTGCAATTTTTATCAAGAAGTAAATATTTTCGATTTTTAT
TTATTTAAGCTAGTGATCTGGCAACTGTGCGGGGCGGCCCTAAAGCTCTGTTTT
TACTGTCTGGTATTTAAACTGAAACAGGTTTCTAAGCAATATGAGGCCACCTT
CAATCCCAAAGTGGGTTGACAGGCCTGGGCCCCCTCCTTGCCCCCTCCCCCTCTGG
AAACATTACTGACCTTTCAAAGAGCTGCCAGCTTTCCTGCACTTTTTACATAA
GAAAAAAGGGGGGGGGGGGAA (SEQ ID NO:1)

FIGURE 1

underlined = deleted in targeting construct

[] = sequence flanking Neo insert in targeting construct

[GCCAGGTCTGGCACCATTGCACTAGGATACCCAGAACGCTGCAAGGCCACGCCCTCCTCAC
 TTCAGGGGTCACCTCTCCCCATTGCCACCACCCACCATTGGCTGGGGATCGGCTCCCGAG
 GAAGGTGATGGACGCAAAGAAA] CTGGCCAGCCTGCTGCGTGGCGGGCCTGGGGGACCCTT
GGTCATCGACAGCCGGTCCTTCGTGGAGTATAACAGCTGCCACGTGCTGAGCTCTGTGAA
TATCTGCTGTTCAAAGCTGGTGAAGCGGCGCCTTCAGCAGGGAAAAGTGACAATTGCTGA
GCTT [ATCCAGCCTGCTACACGGAGCCAG] GTGGATGCCACAGAACCACAGGATGTAGTGGT
 GTATGACCAGAGCACACGAGATGCCAGCGTGCTGGCAGCAGACAGCTTCCTGTCCATCCT
 GCTCAGCAAGCTGGACGGCTGCTTCGACAGTGTGGCCATCCTCACAGGAGGCTTCGCCAC
 CTTCTCCTCCTGCTTCCCTGGCCTCTGTGAGGGCAAGCCTGCCACTCTACCGTCCATGAG
 CCTCTCTCAGCCCTGCCTGCCTGTGCCAGTGTGGCCTGACCCGAATCCTGCCTCACCT
 CTACCTGGGCTCTCAGAAAGATGTCTTGAACAAGGATCTGATGACCCAAAACGGAATAAG
 CTATGTCTCAATGCCAGCAACTCCTGCCCTAAACCGGACTTCATCTGTGAGAGCCGTTT
 CATGCGTATCCCCATCAATGACAACTACTGTGAAAAGCTGCTGCCCTGGCTGGACAAGTC
 CATCGAGTTTATTGATAAAGCCAAGCTGTCCAGCTGCCAAGTCATTGTTCACTGTCTGGC
 TGGCATCTCTCGCTCTGCCACCATTGCCATCGCGTACATCATGAAAACCATGGGCATGTC
 TTCTGACGACGCATACAGGTTTGTGAAGGATCGGCGCCCCCTCCATCTCGCCCAACTTCAA
 CTTCTGGGCCAGTTGCTGGAGTATGAGAGGAGTCTGAAGCTGCTGGCTGCCCTGCAGAC
 TGATGGACCTCACTTGGGGACCCCTGAGCCCTCATGGGCCCCGGCAGCAGGCATCCCACT
 GCCCCGGCTGCCACCATTACCTCAGAGAGCGCTGCCACTGGGAGCGAGGCAGCCACCGC
 AGCCAGGGAGGGCAGCCCAAGTGCTGGAGGGGATGCTCCGATCCCCAGCACAGCTCCAGC
 CACCAGCGCGCTGCAGCAGGGCCTGCGTGGCCTGCACCTCTCCTCTGACCGCCTCCAGGA
 CACCAACCGCCTCAAGCGTTCTTTTTCCCTGGACATCAAGTCGGCCTATGCACCCAGCAG
 GAGGCCCCGACTTTCCCGGCCCCACCGACCCCGGTGAAGCCCCGAAGCTCTGCAAGCTGGA
 CAGCCCGTCTGGGGGCACACTGGGCCTGCCCTCGCCCAGCCCAGACAGCCCGGACTCCGT
 TCCAGAGTGCCGCCCACGACCCCGCCGGCGACGCCCCCGGCTAGTTGCGCTGCCCGCTC
 CCCCCGCGCATGGTCTGGGCCTGAACTTTGGAGACACGGCCCGGCAGACTCCACGGCACGG
 CCTCTCGGCCCTGTGCGCGCCCGGGCTGCCTGGCCCTGGCCAGCCGGCTGGCCCCGGGGG
 CTGGGTGCCGCCACTGGACTCCCCAGGCACACCGTCGCCCCGACGGCCCCCTGGTGCTTCAG
 CCCCAGGGCGCGCAGGGTCCAGGCGCTGTGTTCTCCGCCTTTGGCCGGGTAAGTGCAGG
 CGCACCTGGACCCGGTAACAGCAGCAGCAGCGGTGGTGGTGGTGGTGGTGGTGGCGGCGG
 CGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGG
 CAGCAGCAGCAGCAGCAGCAGTAGTAGTAGTAGTAGTAGTACCTGCGGAGGCGGGATGTGCG
 GACCGGCTGGCCCCGAGGAGCCTGCTGCAGATGCACAGTTCAAGAGGCGCAGCTGCCAGAT
 GGAGTTCTGAAGAGGGCATGGTGGAGGGGCGGGCACGTGGCGAGGAGCTGGCAGCCCTGGG
 CAAGCAAACCAGCTTCTCTGGCAGCGTGGAGGTCATCGAAGTATCGTGACCCTTCAGAAG
 TCCCTGTGCCCTTGCTCCAGCCAGGCCAGGTATAAATATATATTATATATAAAACACACA
 GAAAAGGTAAATGGTTTTACTGCAATTTTTATCAAGAAGTAAATATTTTCGATTTTTTATT
 TATTTAAGCTAGTGATCTGGCAACTGTGCGGGGCGGCCCTAAAGCTCTGTTTTTACTGTC
 TGGTATTTAACTGAAACAGGTTTCTAAGCAATATGAGGCCACCTTCAATCCCAAACCTGG
 GTTGACAGGCCTGGGCCCCCTCCTTGCCCCCTCCCCCTTGGAACATTACTGACCTTTCAA
 GAGCTGCCCAGCTTTCCTGCACTTTTTTACATAAGAAAAAAGGGGGGGGGGAA

FIGURE 2A

Gene Sequence Structure *

Size of full-length
cDNA: 2453 bp

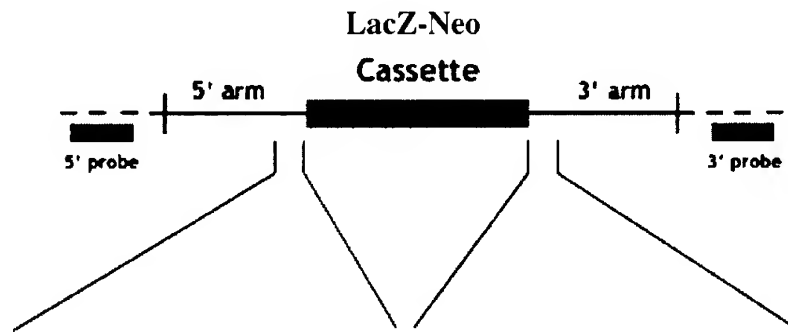
143 bp

Sequence Deleted

304 bp

Targeting Vector* (genomic sequence)

Arm Length:
5': 2.5 kb
3': 2 kb



———— Targeting Vector
- - - - Endogenous Locus

* Not drawn to scale

5' > TCCTGGGAGCCAGCTATAGCT
ACCCAGATCCCACCATCTGCTGAC
TATTCACCTTTCCCCAGGTCTGG
CACCATGCACTAGGATACCCAGAA
CGCTGCAAGGCCACGCCCTCCTCA
CTTCAGGGGTCACTCTCCCATG
CCCACCACCCACCATGGCTGGGG
ATCGGCTCCCGAGGAAGGTGATGG
ACGCAAAGAAA<3'
(SEQ ID NO:2)

5' > ATCCAGCCTGCTACACGAAGC
CAGGTACCTGTGGCCCACCCCTTGC
ATGCGTCTTCAGGGCTGACCATTG
CTGAGCAAACAGACCTATGTCACC
TCTGAAAGAGACAGAGGAGCTCCC
AGGCCTGGTGCCAAGAGTCCTCTG
ATAAGGCATTTCCCCCTCGCTGTC
CCTCCGTTCCAAACAGGGTTCCTT
GGGGTCAGAGC<3'
(SEQ ID NO:3)

FIGURE 2B